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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,651	09/26/2005	Renu B Lal	6395-67675-06	8346

46135 7590 09/06/2007

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EXAMINER	
KINSEY, NICOLE	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
09/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,651	LAL ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *9-11,14-16,18-21 and 24-28* is/are withdrawn from consideration.

5)☒ Claim(s) *17,22 and 23* is/are allowed.

6)☒ Claim(s) *1-8,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse of Group I (claims 1-8, 12, 13, 17, 22 and 23 in the reply filed on June 15, 2007 is acknowledged. The traversal is on the ground that the special technical feature, as now claimed, defines a contribution over the prior art. This is not found persuasive.

The restriction requirement of December 15, 2006 was based on the claims drawn to an isolated recombinant polyepitope polypeptide comprising a plurality of amino acid segments from one or more HIV-1 proteins, wherein two adjacent amino acid segments are linked by a spacer peptide. As stated in the restriction requirement, Duarte et al. teaches each and every one of these limitations. The currently amended claims were not present in the application at the time of the restriction and therefore, the new limitation ("wherein the amino acid segments comprise epitopes selected to be at least 50% sequence conserved across a plurality of HIV-1 subtypes") will not be considered.

In response to applicants' assertion that the special technical feature, as now claimed, defines a contribution over the prior art, applicants are direct to review the claim rejections below.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hanke et al. (WO 01/47955).

The claims are drawn to an isolated recombinant polyepitope polypeptide comprising a plurality of amino acid segments from one or more HIV-1 proteins, wherein two adjacent amino acid segments are linked by a spacer peptide, and wherein the amino acid segments comprise epitopes selected to be at least 50% sequence conserved across a plurality of HIV-1 subtypes.

Hanke et al. teaches polyepitope polypeptides comprising HIV CTL epitopes (see Abstract and Summary). The epitopes are conserved sequences from one or more HIV clades (see page 7, 3rd full paragraph and Table 1 on page 16). The epitopes can have spacers between each epitope or between groups of epitopes (see pages 5-6). Hanke et al. further discloses compositions of the immunogen and additional components such as pharmaceutically acceptable carriers and adjuvants (see page 8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanke et al. as applied to claims 1, 2, 8, 12 and 13 above, and further in view of Velders et al. (The Journal of Immunology, 2001, 166: 5366–5373), Lopalco (U.S. Patent Application No. 2003/0003440) and Carbone et al. (Journal of Immunology, 1987, 138(6):1838-1844).

The claims are drawn to the polyepitope polypeptide further comprising a targeting signal or amino acid segments from one or more HIV-1 co-receptors or a tri-amino acid peptide spacer such as KAA or PGP.

The teachings of Hanke et al. are outlined above. Hanke et al. does not teach a targeting signal, epitopes from a coreceptor or a tri-amino acid peptide spacer.

However, Velders et al. discloses the use of an ubiquitin targeting signal to enhance processing of a polyepitope polypeptide HPV vaccine. Velders et al. found that "ubiquitination of proteins results in increased proteolysis. Since this is a proteasome-mediated pathway, ubiquitination will increase peptide presentation by the

host cells." (see pages 5370 and 5372). Velders et al. further reports the induction of a CTL response and increased CTL precursor frequencies for the vaccines containing ubiquitin at the carboxyl terminus (see discussion). Lopalco teaches the use of CCR5 epitopes to induce antibodies against CCR5 and the use the antibodies to prevent or inhibit HIV infections. With regard to the tri-amino acid spacer, it is well known in the art to use spacers, in particular tri-amino acid spacers, between epitopes (see Velders et al., which used a AAY spacer between epitopes and groups of epitopes, see Figure 1). In addition, Carbone et al. discloses the use of the PGP tri-peptide as a linker in T cell epitopes of a cytochrome c protein (see, for example, page1841).

It would have been obvious to one of ordinary skill in the art to modify the polyepitope taught by Hanke et al. to include an ubiquitination signal. One would have been motivated to do so given the suggestion by Velders et al. that ubiquitination increases proteolysis and ubiquitination induced CTL responses and increased CTL precursor frequencies for the vaccines containing ubiquitin at the carboxyl terminus. There would have been a reasonable expectation of success given the fact that Velders et al. successfully used ubiquitin as part of a HPV vaccine.

It would have been obvious to one of ordinary skill in the art to also modify the polyepitope taught by Hanke et al. to include one or more known epitopes from an HIV co-receptor (CCR5 or CXCR4) binding site. One would have been motivated to do so given the suggestion by Lopalco that antibodies against HIV co-receptor epitopes could block infection (see, for example, paragraph [0004]), and there would have been a reasonable expectation of success given the teachings and findings of Lopalco.

It would also have been obvious to one of ordinary skill in the art to substitute any of the known spacers, in particular tri-peptide spacers as taught by Velders et al. and Carbone et al., in the construct taught by Hanke et al. and the results would have been predictable.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-8, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodberry et al. (Journal of Virology, 1999, 73(7):5320–5325) in view of Suhrbier, (Expert Rev. Vaccines, 2002, 1(2):207-213), Velders et al. (The Journal of Immunology, 2001, 166: 5366–5373), Lopalco (U.S. Patent Application No. 2003/0003440) and Carbone et al. (Journal of Immunology, 1987, 138(6):1838-1844).

Woodberry et al. teaches a polyepitope polypeptide of HIV conserved CTL epitopes from various HIV proteins. The epitopes are conserved over multiple clades (see reference 2 (Brander and Walker) of Woodberry et al., which lists known HIV CTL epitopes and the HIV subtype where each epitope is found www.hiv.lanl.gov/content/immunology/tables/ctl_summary.html).

Woodberry et al. does not teach use of spacers, a targeting signal, epitopes from a coreceptor or a tri-amino acid peptide spacer.

However, Velders et al. discloses the use of an ubiquitin targeting signal to enhance processing of a polyepitope polypeptide HPV vaccine. Velders et al. found that "ubiquitination of proteins results in increased proteolysis. Since this is a

proteasome-mediated pathway, ubiquitination will increase peptide presentation by the host cells." (see pages 5370 and 5372). Velders et al. further reports the induction of a CTL response and increased CTL precursor frequencies for the vaccines containing ubiquitin at the carboxyl terminus (see discussion). Lopalco teaches the use of CCR5 epitopes to induce antibodies against CCR5 and the use the antibodies to prevent or inhibit HIV infections. With regard to the tri-amino acid spacer, it is well known in the art to use spacers, in particular tri-amino acid spacers, between epitopes (see Velders et al., which used a AAY spacer between epitopes and groups of epitopes, see Figure 1). In addition, Carbone et al. discloses the use of the PGP tri-peptide as a linker in T cell epitopes of a cytochrome c protein (see, for example, page1841).

It would have been obvious to one of ordinary skill in the art to modify the polyepitope taught by Woodberry et al. to include a spacer and an ubiquitination signal. One would have been motivated to do so given the suggestion by Suhrbier that the "immunogenicity of individual epitopes might be enhanced by adding appropriate amino acids between the minimal epitopes to improve their proteolytic processing and therefore immunogenicity" and the suggestion by Velders et al. that ubiquitination increases proteolysis and ubiquitination induced CTL responses and increased CTL precursor frequencies for the vaccines containing ubiquitin at the carboxyl terminus. There would have been a reasonable expectation of success given the fact that Suhrbier successfully used spacers and Velders et al. successfully used spacers and ubiquitin as part of their vaccine constructs.

It would have been obvious to one of ordinary skill in the art to also modify the polyepitope taught by Woodberry et al. to include one or more known epitopes from an HIV co-receptor (CCR5 or CXCR4) binding site. One would have been motivated to do so given the suggestion by Lopalco that antibodies against an HIV co-receptor could block infection (see, for example, paragraph [0004]), and there would have been a reasonable expectation of success given the teachings and findings of Lopalco.

It would also have been obvious to one of ordinary skill in the art to substitute any of the known spacers, in particular tri-peptide spacers, in the construct taught by Hanke et al. and the results would have been predictable.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 17, 22 and 23 are free of the prior art and are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E. Kinsey, Ph.D.
Examiner
Art Unit 1648

/nk/

/Stacy B. Chen/ 8-23-2007
Primary Examiner, TC1600